DETAILED ACTION

Claims 1 and 4-24 are pending in the application. Claims 9-24 are withdrawn from consideration. Claims 1, 4-8 are currently under examination.

This Office Action is in response to the amendment filed on 7/28/2010.

Election/Restrictions

Applicant's request for reconsideration of the restriction requirement has been noted. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the requirement is still deemed proper. The finality of this requirement is maintained.

Sequence Compliance

Acknowledgment has been made of Applicant's submission of the sequence listing in both paper and CRF on 11/15/2010. The sequence listing has been accepted and entered into the database on 11/19/2010.

Specification

The objection to the specification has been withdrawn in light of the submitted amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Toby et al (see IDS). **This rejection has been re-written to address the amendment.**

Toby et al. disclose a method of using the classical and modified two hybrid based approaches to study protein-protein interaction. Toby et al. disclose a) transforming a yeast cell expressing a regulatory molecule with a nucleic acid molecule comprising an open reading frame encoding an interaction partner of said biomolecule in expressible form, wherein (i) said regulatory molecule is a nucleic acid binding peptide, a bait that comprises a DNA binding domain from a transcriptional regulator, lexA, (ii) the interaction partner of said regulatory molecule is encoded by a nucleic acid encoding a tagged polypeptide, the prey that comprises nuclear localization sequence, activation domain of B42 and HA tag as fusion to the inserted cDNA, and (b) detecting the reporter readout of lacZ (see page 204, 2nd col., 2nd full paragraph, and Table 1), wherein the reporter readout reflects the expression of the interacting partner (the prey). Toby et al. further disclose split two hybrid system comprising TetR repressor as the binding polypeptide (see for example, Figure 3 and legend). Therefore, Toby et al. disclose the instantly claimed invention.

Response to Arguments

In response to this rejection, Applicant argues that Toby does not teach the claimed method for monitoring the expression level of a gene in a host cell by modulating the activity of a regulatory molecule. Applicant asserts that Toby teaches yeast two hybrid system which is used to detect protein-protein interaction, and neither the bait nor the prey can activate transcription by itself. Applicant asserts that it is the strength of the interaction between bait and prey defines the readout obtained with the reporter system, whereas the claimed invention does

not concern protein-protein interaction. Applicant asserts that the present invention relates to a method that determines the expression level of a gene, wherein a peptide can modulate a regulatory biomolecule, and the peptide is fused to the protein of interest. Applicant asserts that the tag binds and modulates the activity of the regulatory molecule which causes the expression of a reporter gene located downstream of the binding site in the nucleic acid, wherein the expression level of the reporter gene indicates the amount of the tag and the tagged protein. Applicant argues that the teaching of Toby is different from the claimed invention because the interaction between bait and prey causes the transcriptional activation of the colorimetric reporter but that interaction must not release the bait bound to the DNA for the transcriptional activation of the reporter gene to occur. Applicant asserts that the claim limitations of 1 (a) (ii) and (b) have not been met because the claim requires "the interaction partner of said regulatory biomolecule," not the interaction partner of tagged polypeptide. Applicant further asserts that fusing the interaction partner to the activation domain cannot result in any of the nucleic acid molecules in 1 (a)(ii)(1), (2) or (3). Applicant also asserts that it cannot be established by the teaching of Toby that "assessing the expression level of the gene encoding the polypeptide of step a(ii) via a readout system, wherein the readout system is provided by nucleic acid molecule encoding a reporter protein." Moreover, Applicant asserts that Toby teaches TetR as a reporter protein and there is no peptide binding to TetR. Applicant asserts that the present application describes the claimed invention in great detail including extensive experimental data in the form of examples beginning at page 48 of the specification, and such information is missing in Toby. Applicant concludes that the claimed invention cannot be reached by following instruction taught by Toby.

The above argument has been fully considered but deemed unpersuasive. The detailed rejection has been set forth in the previous office action and above. The Examiner acknowledges the difference between the teaching of Toby and the experiments described the specification, however, some of the feature upon which applicant relies is not recited in the rejected claims. For example, applicant's assertion that "the tag binds and modulates the activity of the regulatory molecule which causes the expression of a reporter gene located downstream of the binding site in the nucleic acid" is not part of the claim limitation. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). With regard to the argument directed to claim 1 (a) (i) (ii) and (b), the teaching of Toby clearly meets the claimed limitation. The bait that comprises inserted cDNA fuses to the DNA binding domain of LexA repressor meets the limitation of being a regulatory biomolecule because it is a biomolecule capable of regulating the expression of a reporter gene (the limitation of 1(a)(i)). The prey comprising nuclear localization sequence, B42 activation domain, and HA tag as fusion to inserted cDNA is considered to be the tagged polypeptide, it comprises interacting residue of interaction partner (the cDNA insert that potentially interacts with the bait), wherein the prey is considered to be an tagged interaction partner of the bait because it binds to the regulatory biomolecule and modulates the activity of the bait (the limitation of 1(a)(ii)). The readout system such as the lacZ reporter as taught by Toby is capable of indicating the expression level of the prey when the expression of bait is held constant. In response to applicant's argument that the claimed method has different use as the two hybrid system taught by Toby, Applicant is reminded that a recitation of the intended use of the claimed invention must result in a structural difference

between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case, the disclosure of Toby et al. meets the limitation of every claimed step. With regard to the assertion that Toby lacks the detailed description as set forth in the instant application, Applicant is reminded that such description (supposedly to distinguish the claimed invention from the disclosure of Toby) is not part of the claim limitation. Therefore, for reason discussed in the previous office action and above, this rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Toby et al., in view of Manfredi et al (US 6,828,112).

The teaching of Toby et al. has been discussed above. However, Toby et al. do not teach using antibiotic resistance gene as the reporter protein.

Manfredi et al. teach a method of detecting protein-protein interaction base on the generation of a reporter gene that is detectable when the protein fusion leads to trans-splicing (see abstract). Manfredi et al. teach a number of reporters may be employed in said method including antibiotic resistance gene (see col. 22, lines 50-56, and the bridging paragraph of col. 22 and 23).

It would have been obvious to an ordinary skill in the art reading both the teaching of Toby et al. and Manfredi et al. to realize that antibiotic resistance gene can be employed as the reporter protein in the two hybrid system taught by Toby et al. The ordinary skill in the art would recognize that the antibiotic reporter can be used to positively select host cells expressing the desired bait. The level of skill in the art is high. Absent evidence from the contrary, the ordinary artisan would have reasonable expectation of success to construct a reporter protein linked to a promoter which responds to the binding and activation of the regulatory biomolecule in the presence of the interaction partner. Combining prior art known methods to achieve a predictable results is within the capability of an ordinary skill in the art. Therefore, the claimed invention would have been *prima facie* obvious to an ordinary artisan at the time the invention was made.

Response to Arguments

In response to this rejection, Applicant argues that neither Toby nor Menfredi et al. teach the limitation as set forth in claim 1 (a)(ii)(1), (2) or (3). Applicant asserts the claimed invention would not have been obvious because neither reference teaches or suggests the claimed invention.

The argument has been considered but deemed unpersuasive. The teaching of Toby has taught the limitation of claim 1 (a)(ii)(1), (2) or (3) as discussed above. The claimed invention of using the antibiotic as the readout system would have been obvious in view of the teaching from Manfredi et al. combined with the teaching of Toby for reason given in the rejection. Therefore, for reason discussed in the previous office action and above, this rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CELINE QIAN whose telephone number is (571)272-0777. The examiner can normally be reached on 9:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-2911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Celine X Qian /
Primary Examiner, Art Unit 1636